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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/839,684 | 04/19/2001 | Franklin Okumu | 10466/18 | 1800 |

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| EXAMINER | |
|---|---|
| RUSSEL, JEFFREY E | |
| **ART UNIT** | **PAPER NUMBER** |
| 1654 | |

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/839,684 | OKUMU, FRANKLIN | |
| | Examiner | Art Unit | |
| | Jeffrey E. Russel | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1-52 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 0 216 485 in view of Tipton et al (U.S. Patent No. 5,747,058). The European Patent Application '485 teaches compositions comprising a complex of a growth hormone and a metal, preferably zinc, in combination with a thickened oil vehicle comprising mineral oil or vegetable oil, and optionally in combination with adjuvants or excipients which further extend the release rate of the metal-complexed growth hormone. Preferred oil vehicles are mixtures of peanut oil and aluminum monostearate, and mixtures of soybean oil and beeswax. The molar ratio of zinc to growth hormone is at least 1:1, preferably at least 2:1. The compositions are injected or introduced into an animal as an implant. See, e.g., page 2, lines 20-23; page 3, lines 14-17; and page 3, line 24 - page 4, line 22. The European Patent Application '485 teaches the use of biocompatible thickened oil vehicles in general (see, e.g., page 3, lines 29-32, and claim 10), but does not teach Applicant's particularly claimed carrier material comprising sucrose acetate isobutyrate and a solvent. Tipton et al disclose high viscosity liquid controlled delivery systems comprising a component (HVLCM) that has a viscosity of at least 5,000 cP at 37°C and that does not crystallize neat under ambient or physiological conditions. A preferred component is sucrose acetate isobutyrate (SAIB). The delivery systems can include solvents such as ethanol, propylene carbonate, and benzyl alcohol, which lower the viscosity of the delivery system, e.g. to less than 1000 cP or less than 200 cP, for purposes of administration and which then dissipate or diffuse, leaving a highly viscous implant. Ratios of SAIB:solvent of 60:40 and of 70:30 are exemplified. By selection of the HVLCM and the solvent, a wide variety of pre-

and post-administration composition viscosities can be achieved. The delivery systems can be used for the controlled release delivery of substances such as natural and synthetic bioactive peptides and proteins, including growth factors. The substances to be delivered can preferably be present in amounts ranging from about 2 % to about 10% by weight. See, e.g., the Abstract; column 2, lines 47-67; column 8, lines 16-25 and 41-49; and column 14, lines 1-18. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the delivery system of Tipton et al as the biocompatible thickened oil vehicles of the European Patent Application '485 because the European Patent Application '485 is not limited to the use of any particular biocompatible thickened oil vehicle, because the delivery system of Tipton et al is disclosed to be useful in delivering the same types of biologically active substances, i.e. proteins including growth factors, which are disclosed by the European Patent Application '485, and because use of the delivery system of Tipton et al as the biocompatible thickened oil vehicle of the European Patent Application '485 would have the advantage of providing simple controlled delivery systems which are easily formulated and which provide different pre- and post-administration viscosities for ease of administration (see, e.g., column 2, lines 30-67). Neither the European Patent Application '485 nor Tipton et al teach the exact release rates recited in instant claims 27-30, 32-35, and 37-40. However, the European Patent Application '485 does teach that use of the metal complexes of growth hormone allows a slower release rate upon injection than does the free form of growth hormone (see page 2, lines 7-10), and Tipton et al disclose that release rates can be chosen and optimized by appropriate choice of additives (see column 3, lines 30-44, and column 9, lines 1-5). It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to adjust the

composition of the delivery system in order to optimize the release rates of the European Patent Application '485 as modified above by Tipton et al because the European Patent Application '485 discloses the desirability of a slower release rate upon injection and because Tipton et al disclose that release rate is a result-effective variable and therefore one of ordinary skill in the art would be motivated to optimize such a variable.

3. Applicant's arguments filed January 11, 2005 have been fully considered but they are not persuasive.

The rejection based upon the European Patent Application 0 216 485 in view of Tipton et al (U.S. Patent No. 5,747,058) is maintained. Applicant contends that the references are not properly combinable under 35 U.S.C. 103 because the high viscosity liquid carrier material of Tipton et al does not provide the functions of the oil vehicle of the European Patent Application '485. Applicant states that the purpose of the oil vehicle is to permit injection and to restrict the growth hormone from any available body fluids, whereas the extended release function in the European Patent Application '485 is provided by the metal-complexed growth hormone. The examiner does not agree with Applicant's implication that the thickened oil vehicle of the European Patent Application '485 does not and is not intended to provide extended release function in the compositions of the European Patent Application '485. As noted by Applicant, the thickened oil vehicle of the European Patent Application '485 restricts the metal hormone complex from any available body fluids upon administration to an animal (see page 3, lines 32-35). By restricting the metal hormone complex from any available body fluids, the thickened oil vehicle will cause a slower release rate upon injection, the goal of the European Patent Application '485 (see, e.g., page 2, lines 1-18). Further, the prior art makes clear that oil

vehicles were known to those of ordinary skill in the art to provide extended release function. See, e.g., the WO Patent Application 99/39431 (translated in U.S. Patent No. 6,328,979, column 8, lines 24-28): "In order to further increase the sustained release effect, however, the composition may be formulated with additional components such as vegetable oil, e.g., soybean oil, sesame oil, camellia oil, castor oil, peanut oil, rape seed oil, etc."; U.S. Patent No. 5,889,035 (column 39, lines 50-57): "The highly lipophilic esters, amides and carbamates of the present invention are capable of sustained release in mammals for a period of several days or from about one to four weeks when formulated and administered as depot preparations, as for example, when injected in a properly selected pharmaceutically acceptable oil. The preferred oils are of vegetable origin such as sesame oil, cottonseed oil, corn oil, coconut oil, soybean oil, olive oil and the like"; and U.S. Patent No. 4,016,273 (column 2, lines 20-29): "The compounds of this invention, either in the base form or as the pamoate salts, when incorporated in a formulation containing an injectable oil, with or without a gelling agent such as aluminum monostearate, provide a sustained release (depot) product when administered parenterally. For prolonged action, the compounds are formulated in an injectable oil, preferably a vegetable oil, as for example sesame oil, peanut oil, cottonseed oil, corn oil or soybean oil, or mixtures of these oils". The thickened oil vehicle of the European Patent Application '485 and the HVLCM of Tipton et al do have the same function of providing extended release for the same types of biologically active substances, i.e. proteins including growth factors, with the HVLCM of Tipton et al having the advantage of providing simple controlled delivery systems which are easily formulated and which provide different pre- and post-administration viscosities for ease of administration.

Applicant also contends that the Examples of the specification set forth a probative comparison of unexpected results with a composition that is even closer than that of the European Patent Application '485. The examiner disagrees. The European Patent Application '485 teach a combination of growth hormone, a zinc complexing agent, and a thickened oil vehicle for sustained release. The example in Applicant's specification using the sodium bicarbonate-based formulation is more remote from the claimed invention than the compositions of the European Patent Application '485 which teach the presence of a zinc complexing agent. Further, it is known in the art that complexing human growth hormone with zinc suppresses the initial burst in sustained release compositions. See Yamagata et al, U.S. Patent No. 6,191,107, already of record. Thus the example in Applicant's specification merely confirms what is already known about zinc complexing agents, and does not constitute evidence of unexpected results.

The rejection based upon Jeng et al (U.S. Patent No. 6,719,992) is withdrawn. As demonstrated by Applicant in the response, the sucrose stearate and sucrose distearate of Jeng et al are not liquids which satisfy the functional requirements of the claimed carrier materials. Further, at least for claims 1, 2, and 26, these claims are entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/198,209 for the reasons given in Applicant's response, and Jeng et al is not prior art against at least claims 1, 2, and 26.

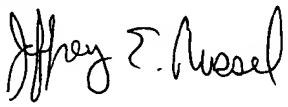
4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

February 4, 2005